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The thalamus and language revisited

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ABSTRACT

Regionalization of language function within the left thalamus has been established with language and verbal memory effects of thalamic stimulation during surgery for movement disorders. Three distinct language effects of thalamic stimulation were established: anomia from posterior ventrolateral (VL) and pulvinar regions; perseveration from mid-VL regions; and, a memory and acceleratory effect from anterior VL, described as a “specific alerting response” (SAR). These studies are reviewed in context of pertinent contemporary and recent literature on the thalamic role in memory and language. An explicit mechanistic model for the anomia and SAR effect is proposed. The suggested model for the SAR effect involves secondary switching in the striatum by the activation of thalamostriatal projections, whereas the anomia effect implicates the disruption of the cortical synchronization action of pulvinar via the cortico-pulvinar–cortical projection system. Further experimental data is required to firmly establish these mechanisms.

1. Introduction

In 1975, the then editor of Brain and Language, Harry Whitaker, asked one of us (GAO) to be guest editor for a special volume on the “Thalamus and Language” (Ojemann, 1975b). Although suggestions that the thalamus might have a specific language role were made early in the history of aphasiology (Dejerine & Roussy, 1906; Marie, 1906), the prevailing view until the 1960s was that the thalamus had no role beyond that associated with the maintenance of overall alertness (Neilsen, 1946). Two distinct developments in the decade prior to the Brain and Language 1975 “state of the art” review challenged that view. The first evidence came from the ability to more frequently identify spontaneous thalamic lesions during life and thus assess language function (Fisher, 1959), particularly with the advent of computerized tomographic scanning (Mohr, Watters, & Duncan, 1975); further was the recognition of language deficits independent of changes in general alertness after stereotaxic thalamic lesions placed for the treatment of movement disorders (Bell, 1968; Selby, 1967). The evidence from both approaches suggested lateralization of thalamic function with a special language role for left thalamus. Moreover, the stereotaxic procedures provided an opportunity to investigate that role in more detail, using electrical stimulation mapping techniques that had been developed by Penfield to map cortical language localization (Penfield & Roberts, 1959), and was the focus of the investigations by one of the authors and his colleagues (Ojemann, Fedio, & Van Buren, 1968 and subsequently). The present paper reviews the findings from those studies and the models for specific thalamic roles in language derived from them. Those models are evaluated in light of newer evidence, particularly functional neuroimaging and the opportunities provided by the renewed interest in stereotaxic thalamic surgery using chronic electrical stimulation instead of lesions.

2. Review of original studies

The studies from the 1960s and 1970s of one of the authors were conducted during the stereotaxic placement of lateral thalamic lesions for movement disorders in patients awake for clinical reasons under local anesthesia. Although the effective targets are much more refined today, at that time the ideal thalamic target had not yet been defined (Ojemann & Ward, 1973), and there continues to be equipoise today for targets for Parkinson’s Disease and Essential Tremor (Follett et al., 2010; Hamel et al., 2007). As a result, a number of different approaches and targets within lateral thalamus were explored, including more dorsal portions of the ventrolateral (VL) nuclear mass and a posterior approach that provided an opportunity to assess the superior portion of pulvinar (Fig. 2). The initial electrical stimulation mapping studies conducted during these procedures assessed semantic language function with object-naming paradigms using objects with names that were common nouns. This was a direct extension to the lateral

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thalamus of the Penfield technique for cortical language mapping. All paradigms included interspersed control trials without stimulation. Studies occurred after initial placement of the electrode into the presumed target and before any correction or lesion placement. Anatomical targets were defined in relation to landmarks within the third ventricle, including anterior and posterior commissures. Atlases derived from anatomic specimens with statistical maps of thalamic boundaries about those landmarks provided a mechanism for establishing electrode location within thalamus with reasonable certainty (Van Buren & Borke, 1972). Direct visualization of thalamic nuclei has only been possible with the much more recent advent of magnetic resonance imaging (MRI). Stimulation was performed using a square charge-balanced symmetrical current waveform with pulse width of 1 ms at a frequency of 60 Hz and pulse train length up to 9 s. Stimulation was delivered in a monopolar mode for all but the earliest studies through a cylindrical electrode (1 mm diameter, 5 mm length).

2.1. Language effects of thalamic stimulation

For electrodes with a high probability of being within lateral thalamus, all evoked changes in naming were confined to the left thalamus, see Fig. 1 (Ojemann, 1977) and Table 1. Three different patterns of naming changes were identified, with different localization within left lateral thalamus:

1. *Anomia effect:* From electrodes in posterior portion of VL nucleus and the adjacent anterior superior pulvinar, errors in naming with a retained ability to speak, as indicated by the ability to read the phrase "this is a" printed above the object picture, were evoked (A, Fig. 1). The majority of these errors were omissions, the remainder random misnamings. Although obtained in two different patient series, the pattern in the pulvinar and posterior VL locations was similar (Ojemann & Ward, 1971; Ojemann et al., 1968). In the pulvinar series, the latency of correct naming was also examined and found to be significantly slowed with stimulation.
2. *Repetition effect:* From electrodes in anterior VL, a different pattern of naming errors was evoked. Above a threshold current, the same wrong name was repeated for each object stimulated (R, Fig. 1). This was commonly the last object correctly named at a subthreshold current (Ojemann, 1975c). Latency for correct naming was slightly (but not significantly) shortened (Ojemann, 1974). These changes were related to a "specific alerting response", discussed below.
3. *Perseveration effect:* Between these two patterns of naming errors were several patients with sites where stimulation evoked perseveration on the first syllable of the correct object name (P, Fig. 1). This effect was related to a thalamic role in integrating non-symbolic motor aspects of speech also discussed further below. These same subjects demonstrated symbolic language errors (anomia) at higher stimulating currents.

The anomic and syllabic perseverative errors were similar to those evoked from lateral cortex (Corina et al., 2010) but repetition errors were rarely seen from cortex. Within left thalamus no naming errors were evoked from the most posterior medial inferior electrodes (Fig. 1). For some electrodes within the range of variation of the lateral border of either thalamus an arrest of all speech was evoked, likely representing current spread to corticobulbar tracts in the adjacent internal capsule (Ojemann, 1975c). The localization of different aspects of language to subdivisions of left thalamus was determined using summaries of electrode locations across the subject population.

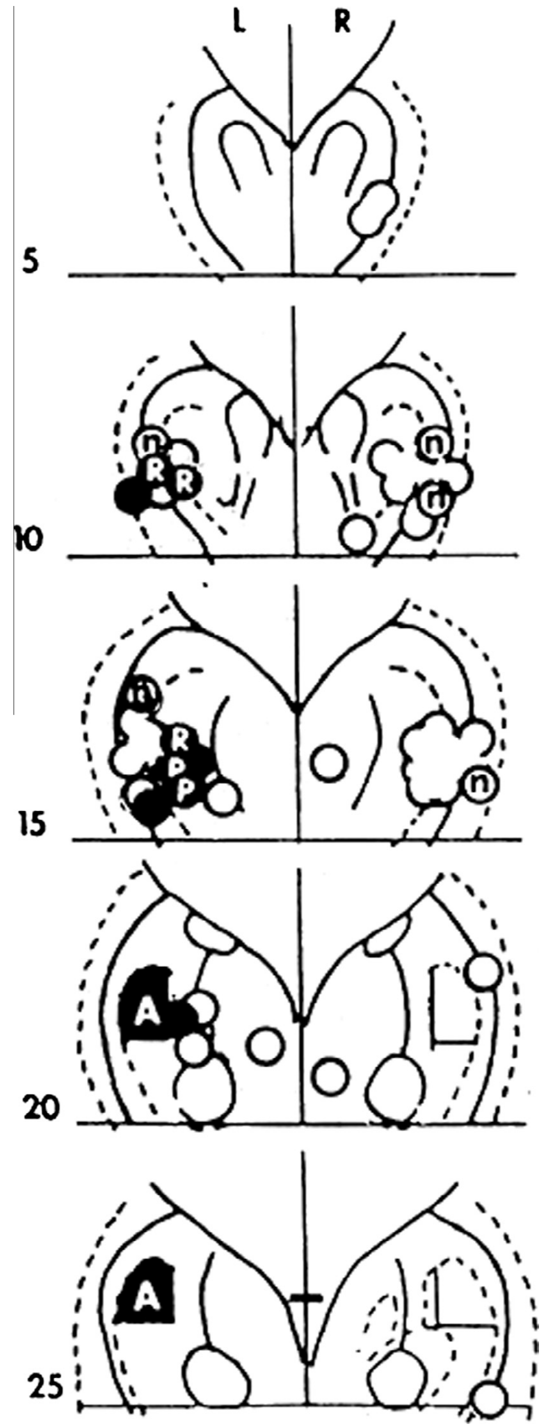

Fig. 1. Coronal sections of the thalamus from 5 to 25 mm posterior to the anterior commissure, indicating the location of electrodes included in the studies of Ojemann et al. (1971, 1977) on stimulation effects on object naming (ON). These coronal sections, adapted from the atlas of Van Buren and Borke (1972) indicate the mean location and 90% range of variation of the thalamic landmarks in relation to the intercommisural plane (horizontal line) and the midline of the brain (vertical line), the same landmarks used for electrode localization. The effect on ON evoked by 60 Hz stimulation of that electrode at currents up to the sensory threshold are indicated by symbols: Open circle: no effect; Shaded: arrest of all speech, Filled without letter: anomic ON error; Filled with "R": anomic errors characterized by repetition of a specific wrong name above a threshold current; Filled with "P": perseveration on the first syllable of the correct name. Cross hatched area indicates the area where anomia was evoked in a separate series of patients (Ojemann et al., 1968). The cross mark on the vertical line of the 25 mm section is 1 cm above the horizontal line. Figure adapted from (Ojemann, 1977).